

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
17 January 2002 (17.01.2002)

PCT

(10) International Publication Number
WO 02/03968 A1

- (51) International Patent Classification⁷: **A61K 9/48**
- (21) International Application Number: **PCT/GB01/02766**
- (22) International Filing Date: **21 June 2001 (21.06.2001)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:
PCT/GB00/02616 7 July 2000 (07.07.2000) GB
0109089.3 11 April 2001 (11.04.2001) GB
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Declaration under Rule 4.17:**
— of inventorship (Rule 4.17(iv)) for US only
- Published:**
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 02/03968 A1

(54) Title: **DELIVERY CAPSULES**

(57) Abstract: A delivery capsule has an enclosing wall comprising a thermoplastic film of foamed modified cellulose material, preferably hydroxypropyl methyl cellulose. The foamed material dissolves rapidly in the mouth of a consumer, releasing the capsule contents into the consumer's mouth.

Title: Delivery CapsulesField of the Invention

This invention relates to a delivery capsule, that is, a capsule designed to retain and protect its contents until an intended site of delivery or conditions of delivery are encountered, at which point the capsule contents are released.

Background to the Invention

Delivery capsules are well known and find particular application in the form of ingestible gelatin capsules for the delivery of accurately metered doses of pharmaceutical preparations and dietary supplements. Liquid preparations are typically encapsulated in soft gelatin capsules and particulate or powdered preparations are typically encapsulated in two part hard gelatin capsules. The capsules are designed to release their contents after ingestion, typically by solution of the capsule wall at a location in the digestive system of a consumer. By use of suitable capsule material such capsules can thus provide a means of administering a dose of a preparation at a desired appropriate site in the body. The finished capsules offer protection to the contents yet solubility within the body.

Summary of the Invention

In one aspect the invention provides a delivery capsule having an enclosing wall comprising a thermoplastic film of foamed modified cellulose material.

The modified cellulose material is preferably hydroxypropyl methyl cellulose (HPMC), which is a synthetic thermoplastic material that is a modified form of the naturally occurring polymer cellulose. Other modified cellulose materials include hydroxypropyl cellulose (HPC).

In a preferred aspect the invention thus provides a delivery capsule having an enclosing wall comprising a thermoplastic film of foamed hydroxypropyl methyl cellulose.

Modified cellulose materials are suitable for ingestion by humans, so the delivery capsules of the invention are suitable for human consumption.

The material is foamed, that is, the material includes a plurality of small openings, pockets or voids within the body of the material. The voids are typically filled with gas, commonly air, oxygen or carbon dioxide, but preferably nitrogen, although the voids may be empty. The voids should be small (typically having a maximum dimension in the range 1 to 100 microns) and are ideally substantially uniform in the size and are preferably reasonably uniformly dispersed through the material, for uniformity of properties. Foamed material may also be referred to as expanded material, gasified material or aerated material.

The void volume of the foamed material should be selected to give desired properties. Generally the void volume is in the range 20 to 60% by volume, typically being about 50% by volume.

Foamed modified cellulose materials, with a controlled desired void level, can be readily made, e.g. by mechanical entrainment of gas, such as nitrogen, in appropriate quantity in a liquid to be used for production of a cast film.

The film material typically includes a plasticiser to give desired properties of flexibility to the film, in known manner. Materials used as plasticisers include polyethylene glycol (PEG), monopropylene glycol, glycerol and also acetins, which are acetates of glycerol.

The film typically has a thickness in the range 50 to 200 microns, e.g. in the range 140 to 150 microns, with film thickness being controllable in known manner. Films of different thickness may be suited to different uses.

It is surprisingly found that the presence of voids in the foamed film results in the film rapidly starting to dissolve in the mouth of a consumer, possibly after only a few seconds of

chewing or sucking, resulting into release into the mouth of the capsule contents. The release time varies depending on wall material, thickness and void volume, and is usually less than one minute, typically less than 30 seconds and possibly much shorter than that, e.g. only a few seconds. The film material dissolves completely relatively soon after this, e.g. after a minute or so. The time for total dissolution varies depending on capsule size, content and wall thickness. This behaviour is to be contrasted to that of non-foamed film of the same thickness which dissolves more slowly in the mouth. The foamed film used in the present invention also has organoleptic properties in the mouth generally regarded as pleasant, providing a "melt-in-the-mouth" sensation, similar to that of eating rice paper.

Capsules in accordance with the invention find application as capsules intended for use in delivery of contents to the oral cavity of a user, for instance with the contents being in the form of a foodstuff such as confectionery or a medication such as a unit dose of a throat-treatment liquid. In use of such capsules, the capsule wall starts to dissolve very rapidly after introduction to the mouth, possibly after sucking or chewing, releasing the contents into the mouth. The capsule wall material is pleasant to chew and dissolves completely in the mouth after a short time.

In a preferred aspect the invention thus provides an edible delivery capsule having an enclosing wall comprising a thermoplastic film of foamed modified cellulose material, preferably hydroxypropyl methyl cellulose, and capsule contents for release into the mouth of a consumer.

In contrast to known ingestible delivery capsules that are intended to be swallowed whole, with the capsule contents being released in the digestive tract of the consumer, the capsules of the invention are intended to be ruptured in the mouth of the consumer for release of contents into the mouth.

The enclosing wall is preferably made entirely or substantially entirely from thermoplastic film of foamed modified cellulose material, so that the entire wall can dissolve relatively rapidly in the mouth of a consumer.

The film may include optional colourings, e.g. in the form of known food dyes such as F D and C yellow number 5, optional flavourings, e.g. sweetenings, textures etc, in known manner. The film may also optionally include an acidulant material, such as citric acid, for improved mouth feel.

The capsule contents may be solid, e.g. in the form of a powder, granules, particles or a waxy solid etc, or liquid. In the case of liquid contents, because the film material is cold water soluble, these should contain little or no free or unbound water as otherwise the capsule wall will dissolve prematurely. However, bound water, e.g. as present in a carbohydrate solution such as an syrup, is acceptable, up to levels of about 40% of the weight of the liquid contents.

The capsules may optionally include one or more edible outer coatings, on top of the enclosing wall, e.g. in the form of a candy coating.

Although the film material is cold water soluble, the capsules are nevertheless found to be reasonably robust and will withstand a certain amount of handling, including being held in the hand, without the wall dissolving or rupturing prematurely.

The capsules may have a range of different sizes and shapes as appropriate dependent on intended usage. Capsules are typically generally spherical, ovoid, cylindrical etc. in shape. Typically the maximum dimension of the capsule is in the range 3mm to 50mm, but other sizes are possible. Where the capsule is intended to carry a unit dose, e.g. of a medication, the capsule can be appropriately sized to carry the desired dose.

The capsule may be compartmented, as described in WO 01/03676.

In a further aspect the invention thus provides a delivery capsule having at least two separate chambers, wherein at least part of the capsule wall comprises a thermoplastic film of a foamed modified cellulose material, preferably hydroxypropyl methyl cellulose.

In such compartmented capsules, some or all of the enclosing wall may comprise a thermoplastic film of foamed modified cellulose material, preferably hydroxypropyl methyl cellulose.

Capsules in accordance with the invention may be made in generally conventional manner, e.g. as disclosed in WO 97/35537, WO 00/27367 and WO 01/03676.

The invention will be further described, by way of illustration, in the following example.

Example

A foamed hydroxypropyl methyl cellulose film was made, having the following composition by weight:

Hydroxypropyl methyl cellulose	77%
Polyethylene glycol (plasticiser)	23%

The film was made in generally conventional manner. HPMC, in the form of a powder, was mixed with PEG and water to produce an aqueous solution, with stirring. The solution was gasified to a desired extent by addition of nitrogen gas in known manner.

The gasified solution was then fed to a feed hopper, including an elongate exit slot located a small distance above the upper surface of a moving conveyor belt adjacent one end thereof, with the slot extending perpendicularly with respect to the direction of movement of the belt. The feed arrangement geometry and speed of movement of the belt were such that a layer of liquid of desired thickness was applied to the belt and was moved on the belt away from the feed hopper, forming a film. The film was passed on the belt through a heating zone in which hot air heated the film, driving off water and so drying the film. The resulting dried, cast foamed HPMC film was removed from the belt and wound onto reels. The dried film had a thickness of about 150 microns, with a void volume of about 50%.

Edible delivery capsules were made from the film, e.g. as described in WO 97/35537, WO 00/27367 and WO 01/03676.

In one embodiment the capsules are in the form of a confectionery product, with the capsules being generally spherical with a diameter of about 20mm and containing a liquid chocolate or syrup formulation. On insertion into the mouth of a consumer, the foamed HPMC film starts to dissolve very rapidly, after a few seconds, releasing the liquid contents into the mouth. The film dissolves completely after about one minute, possibly assisted by sucking or chewing. The film has pleasant mouth-feel properties.

In another embodiment, the capsules are of similar form and size but contain a unitary dose of a medicated throat treatment liquid. In use, the liquid is rapidly released into the mouth of the consumer for contact with the throat region.

Claims

1. A delivery capsule having an enclosing wall comprising a thermoplastic film of foamed modified cellulose material.
2. A capsule according to claim 1, wherein the film comprises hydroxypropyl methyl cellulose.
3. A capsule according to claim 1 or 2, wherein the foamed material has a void volume in the range 20 to 60% by volume.
4. A capsule according to claim 1, 2 or 3, wherein the film has a thickness in the range 50 to 200 microns.
5. An edible delivery capsule having an enclosing wall comprising a thermoplastic film of foamed modified cellulose material, and capsule contents for release into the mouth of a consumer.
6. A capsule according to claim 5, wherein the film comprises hydroxypropyl methyl cellulose.
7. A capsule according to any one of the preceding claims, further comprising one or more edible outer coatings, on top of the enclosing wall.
8. A delivery capsule having at least two separate chambers, wherein at least part of the capsule wall comprises a thermoplastic film of a foamed modified cellulose material.
9. A capsule according to claim 8, wherein the film comprises hydroxypropyl methyl cellulose.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/02766

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 110 502 A (WARNER-LAMBERT COMPANY) 13 June 1984 (1984-06-13) claims 1-16	1-9
A	US 2 810 659 A (GREMINGER ET AL.) 22 October 1957 (1957-10-22) the whole document	1-9



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

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L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

8 document member of the same patent family

Date of the actual completion of the international search

2 October 2001

Date of mailing of the international search report

09/10/2001

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 01/02766

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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